REMARKS

Claims 1-6 were in the application as originally filed. Claims 7-12 were added in the amendment filed on December 11, 2003. Claims 1-12 remain in the application.

Claim 2 has been amended in order to correct an obvious typographical error.

Claims 2 and 3 have been amended to delete the chemical formula labels.

Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph. In support of this rejection the Examiner has stated that:

> Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of "diabetic neuropathies, polyarthritis, arthrosis, lumbago, and traumatological pain," does not reasonably provide enablement for treatment of "inflammation", "the symptomatic treatment of painful conditions of light to moderate intensity and/or feverish states" and "inflammation in the ENT field." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.
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> There are no known compounds of similar structure which have been demonstrated to treat all types of inflammatory diseases or conditions. For instance, many types of cancers (e.g., bladder, colon, pancreas, stomach, etc...) are characterized by inflammation. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different method of growth and harm to the body. Also see In re Buiting, [sic] 163 USPQ 689 (CCPA 1969), wherein "evidence involving a single compound ant [sic] two types of cancer, was held insufficient to establish utility of the claims directed to disparate cancers.' Thus, it is beyond the skill of oncologists/clinicians today to get an agent effective against all types of cancers and/or inflammatory diseases in general. Since applicant's assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology.
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> The claims are very broad. The breadth of the claims not only includes the disclosed examples of diabetic neuropathies, polyarthritis, arthrosis, lumbago and traumatological pain, but also pancreatitis, ALS, Alzheimer's disease, cachexia/anorexia, asthma, diabetes, glomerulonephritis, graft versus host rejection, hemorrhagic shock,

> hyperalgesia, inflammatory bowel disease, cancers (e.g., mouth cancer, esophageal cancer, lip cancer, colorectal cancer, brain cancer, liver cancer, etc...), psoriasis, contact dermatitis, etopic eczema, reperfusion injury, septic shock, multiple sclerosis, cerebral ischemia, bursitis, allergic neuritis, etc...
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> The specification discloses the use of succinic acid derivatives represented by the formula as an agent that is useful for the treatment of inflammation. As the specific embodiment of the claimed invention, (s)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionic acid was tested in an experimental model of plantar inflammation in rats, and found to exhibit anti-inflammatory (page 3, line 20 thru page 5, line 12).
> However, there is no demonstrated correlation that the tests and results apply to all of the disorders or disease conditions embraced by the instant claims. The specification fails to provide sufficient information allowing the skilled artisan to envision the desired result of the claimed invention without undue amount of experimentation.
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> The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in the determining whether "undue experimentation" is required to make and use the instant invention. "the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed."
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> For these reasons, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine all of the "inflammation," "the symptomatic treatment of painful conditions of light to moderate intensity and/or feverish states" and "inflammation in the ENT filed" that would enabled in this specification.

This rejection is traversed and reconsideration and withdrawal thereof is respectfully requested for the reasons given hereinbelow.

Claim 1 is directed to a method of treating inflammation comprising administering to a patient in need of such treatment an effective amount of a compound of general formula (I), and, hence, is clearly limited to a method of "treating inflammation" (See e.g., *Rappoport v. Dement*, 59 USPQ2d 1215 (Fed. Cir. 2001)). Each of rejected claims 2 to 12 depend directly or indirectly from claim 1, and therefore carry the same limitation. However, the Examiner's main argument appears to be that, to the extent that any illness associated with inflammation is embraced by the

claim language (such as cancer, multiple sclerosis, ALS, asthma, graft versus host rejection, etc.), the claims are read to broadly encompass methods of treating these illnesses, and, as a result, the disclosure must be enabling for treatments of such illnesses. This misinterpretation of the claims is apparent by the evidence provided by the Examiner in support of the instant rejection which relate broadly to methods of treating various diseases and disorders, and not to the more limited methods of treating inflammation.

For instance, the Examiner equates methods of treating cancer with the claimed methods of treating inflammation by stating that many types of cancers are characterized by inflammation. Applicant notes that the Examiner provides no documentary evidence to support this "characterization." Nevertheless, such a "characterization" alone does not expand the claims to embrace "methods of treating cancer." The Examiner's conclusion that "it is beyond the skill of oncologists/clinicians today to get an active agent to be effective against all types of cancers and/or inflammatory diseases" affirms that the Examiner has attempted to broaden the meaning of instant claims to include such "methods of treating cancer." The claims are not so broad, as they are limited to administration of succinic acid compounds for the treatment of inflammation, to a person in need thereof.

The Examiner also cites the Cecil Textbook of Medicine which describes that "[a]ll cancers invade or metastasize, but each type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment, and study." While this may be true, this reference is completely unrelated to the claims at bar. The rejected claims are not directed to diagnosing, treating or studying cancer, but, on their face, are clearly limited to methods of treating inflammation to patients in need of such treatment. Therefore, the cited reference clearly adds nothing to the instant rejection.

The Examiner also relies on *In re Buting* (163 USPQ 689 (CCPA1969)) wherein evidence involving a single compound in the treatment of two types of cancer was held insufficient to *establish utility* of the claims directed to disparate cancers. However, the claims of *Buting* are clearly distinguishable to those of the instant invention in that the *Buting* claims are directed to methods of treating malignant conditions (cancer), whereas the instant claims are

directed to treating inflammation to a person in need of such treatment. Applicant again emphasizes that the claims are not directed methods of treating "all types of cancers" and therefore, the Examiner should not require that the specification be enabling for treating all types of cancer.

Lastly, the Examiner indicates that there is no demonstrated correlation that the tests described in the instant specification apply to "all of the disorders or disease conditions embraced by the instant claims." Applicant respectfully submits that the instant claims only embrace methods of treating inflammation in patients in need such treatment, which are further limited by dependent claims 2-12, and do not embrace methods of treating "all of the disorders or disease conditions" which may cause such inflammation. That inflammation may be implicated in several different diseases or disorders does not make the claims non-enabled.

For the reasons given hereinabove, Applicant respectfully submits that the Examiner has failed to establish a prima facie case of non-enablement, and withdrawal of the rejection of claims 1-12 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 2-3 and 5-6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In support of the rejection, the Examiner has stated that:

> Dependent claims 2-3 limit the independent claim 1 by reciting "the compound of formula (I) is compound..." The subgenus structures shown in claims 2-3 are depicted with (I) as the claimed structure in claim 1. The formula (I) structure shown in claim 1 differs from the structures in claim 2 and 3 labeled as the structure (I). This inconsistency in the claims makes the claimed subject matter vague and indefinite. Claims 5-6 are also rejected because they are depending on the rejected base claims.

Without acquiescing in the propriety of the rejection, and solely to advance prosecution, Applicant has amended claims 2 and 3 to delete the labels of (I) for the subgenus compounds of Formula (I). Therefore, this rejection is believed overcome and withdrawal thereof is respectfully requested.

Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sato et al. (EP 050734), for the stated reason that:

> Sato teaches use of the claimed succinic acid derivatives represented by the formula (e.g., (s)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl) propionic acid) having hypoglycemic activity for the treatment of diabetes (abstract; Example 41).
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> Since the broadly interpreted "inflammation" encompasses various disorders that are mediated or manifested by inflammation including diabetes, the reference anticipates the claimed invention.

This rejection is traversed and reconsideration and withdrawal thereof is respectfully requested.

It is well established that anticipation requires that each and every element set forth in the claim be present, either explicitly or inherently, in a single prior art reference. For this reason, in order to anticipate a claim reciting the use of an agent to treat a particular disorder in a patient in need thereof, the prior art must disclose the use of that agent with the *intent or purpose* of treating the claimed disorder (see e.g., *Rapoport v. Dement,* 59 USPQ2d 1215 (Fed. Cir. 2001); *Jansen v. Rexall Sundown Inc.*, 68 USPQ2d 1154 (Fed. Cir. 2003)). Therefore, in order for the teachings of Sato et al. to anticipate claims 1-4, the patent must describe a method of treating inflammation in a patient in need thereof.

Sato et al. describes succinic acid compounds that exhibit hypoglycemic activity, and as such, are taught to be useful for the treatment of diabetes because the compounds enhance insulin secretion to reduce blood glucose levels. The instantly claimed invention is *not* directed to a method of treating diabetes, but is directed to methods of treating inflammation in a patient in need thereof. Since Sato fails to describe the use of the succinic acid derivatives for the purpose or with the intent of treating inflammation in a patient in need thereof, than each and every element set forth in the rejected claim is clearly not present in the Sato reference.

It appears as though the Examiner is construing the claims to broadly encompass methods of treating "disorders that are mediated or manifested by inflammation" including methods of treating diabetes. However, this reading of the claims ignores that the claims are limited to methods of treating inflammation in a person in need thereof. Sato clearly does not describe any

methods of treating inflammation or any person who may need such treatment, and, consequently, the disclosure contained in the cited patent cannot possibly anticipate the instant claims. Accordingly, the rejection of claims 1-4 under 35 U.S.C. § 102(b) is believed to be unwarranted and should, therefore, be withdrawn.

Claims 5-12 are rejected under 35 U.S.C. § 103(a) for being unpatentable over Sato et al. in view of NIH Publication No. 95-3185, 1995: "Diabetic Neuropathy: The Nerve Damage of Diabetes." In support of this rejection the Examiner has stated that:

> NIH Publication No. 95-3185 teaches that the treatment of diabetic neuropathy aims to relieve discomfort and prevent further tissue damage. The reference discloses "the first step is to bring blood sugar under control by diet and oral drugs or insulin injections, if needed, and by careful monitoring of blood sugar levels...maintaining lower blood sugar levels helps reverse the pain or loss of sensation that neuropathy can cause. Good control of blood sugar many [sic] also help prevent or delay the onset of further problems."
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> The teaching of Sato differs from the claimed invention in the use of said compound of the formula such as (s)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)proprionic acid for the "symptomatic treatment of painful conditions of light to moderate intensity and/or feverish states", namely "treatment of diabetic neuropathies, polyarthritis, arthrosis, lumbago, traumatological pain and inflammation in the ENT field". To incorporate such teaching into the teaching of Sato, would have been obvious in view of NIH Publication No. 95-3185 that teaches the importance of maintaining lower blood glucose levels in treating or reversing symptoms of diabetic neuropathy (e.g., pain or loss of sensation) by oral hypoglycemic drug, diet or insulin injection.
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> One having ordinary skill in the art at the time of the invention was made would have expected that good control of blood glucose with the administration of oral hypoglycemic drug would provide beneficial effect in the treatment of diabetic neuropathies or symptomatic treatment of painful conditions of light to moderate intensity. One having ordinary skill in the art would have expected that the administration of said compound having hypoglycemic activity is useful for the treatment or symptomatic treatment of painful conditions of light to moderate intensity, namely diabetic neuropathies. Therefore, one having ordinary skill in the art would have been motivated to make such modification, with the reasonable expectation of success, to extend usage of said compound (e.g., (s)-2-benzyl-3-(cis-hexahydro-2-isoindolinylcarbonyl)proprionic acid) to accommodate patient's preference and needs where the more effective treatment is desired. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields

(constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

This rejection is traversed and reconsideration and withdrawal thereof is respectfully requested.

To establish a prima facie case of obviousness, the prior art must teach or suggest *all of the claim limitations*. In this regard, Applicant notes that each of the instantly rejected claims 5-12 depend directly or indirectly from independent claim 1, and hence carry the same limitations as claim 1. Therefore, to establish a prima facie case of obviousness, the prior art must at least teach or suggest a method of treating inflammation which comprises administering to a patient in need of such treatment an effective amount of a compound of formula I, as required by claim 1.

The primary reference, Sato et al. describes succinic acid compounds that exhibit hypoglycemic activity, and as such, are taught to be useful for the treatment of diabetes because the compounds enhance insulin secretion to reduce blood glucose levels. Nowhere do Sato et al. teach or suggest the use of such compounds for the treatment of inflammation, let alone methods of treating inflammation for the symptomatic treatment of painful conditions of light to moderate intensity and/or feverish states; or for the treatment of inflammation for the treatment of diabetic neuropathies, polyarthritis, arthrosis, lumbago, traumatological pain and inflammation in the ENT field as required by the instantly rejected claims.

The secondary NIH reference, teaches that maintaining low blood sugar levels helps reverse the pain or loss of sensation the nerve damage of diabetic neuropathy can cause. The Examiner concludes that it would have been obvious to one of skill in the art to use the compounds of Sato et al., which are taught to have hypoglycemic activity, in the treatment of diabetic neuropathy or symptomatic treatment of painful conditions of light to moderate intensity. However, neither of the cited references, either alone or in combination, teaches or suggests methods of treating inflammation by administering to a patient in need thereof one of the succinic acid derivatives embraced by the instant claims. In fact, the Examiner has not even alleged that methods of treating inflammation would be obvious by the combined teachings of the NIH publication and Sato et al. The Examiner has also failed to establish what would have motivated one of ordinary skill in the art to use any hypoglycemic agent, let alone those of the

instant invention, for the treatment of inflammation. Since the combined teachings of Sato et al. and the NIH publication plainly fail to teach or suggest each of the claim limitations set forth in the instantly claimed invention, one skilled in the art would not have been led to Applicant's claimed invention. Therefore, the claimed invention would not have been obvious to such a person at the time the invention was made and, hence, the rejection of claims 5-12 under 35 U.S.C. §103(a), based on said references is believed to be unwarranted and should be withdrawn.

In view of the foregoing amendments and remarks, reconsideration and withdrawal of: (a) the rejection of claims 1-12 under 35 U.S.C. § 112, first paragraph, (b) the rejection of claims 2-3 and 5-6 under 35 U.S.C. § 112, second paragraph, (c) the rejection of claims 1-4 under 35 U.S.C. § 102(b), and (d) the rejection of claims 5-12 under 35 U.S.C. § 103(a) is requested and allowance of claims 1-12 is respectfully requested.

Respectfully submitted,

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